Division of Medicaid

Office of the Governor

State of Mississippi

DUR Board Meeting

November 20, 2008

2:00 p.m.

Woolfolk Building, Room 117

Jackson, MS

Drug Utilization Review Board

Roy L. Arnold, Jr., R.Ph.
Clayton Drug Store
216 Main Street
Collins, MS 39428-0787
Term Expires: June 30, 2009

Laura Gray, M.D.
905 Garfield Street
Tupelo, MS 38801
Term Expires: June 30, 2009

John M. Wallace, M.D.
Jefferson Medical Clinic
1203 Jefferson Street
Laurel, MS 39440
Term Expires: June 30, 2009

Lee Voulters, M.D.
1340 Broad Ave Suite 440
Gulfport, MS 39501
Term Expires: June 30, 2009

Edgar Donahoe, M.D.
Indianola Family Medical Group
122 Baker Street
Indianola, MS 38751
Term expires: June 30, 2010

Mark Reed, M.D.
University of Mississippi Medical Center
2500 North State Street, Trailer 16
Jackson, MS 39216
Term expires: June 30, 2010

Lee Merritt, R.Ph.
Medfusion
2211 5th Street North
Columbus, MS 39705
Term expires: June 30, 2010

Vickie Veasey, R.Ph.
MS State Hospital at Whitfield
Building #50
Whitfield, MS 39193
Term Expires: June 30, 2010

Frank Wade, M.D.
Family Medical Clinic
376A Simpson Highway 149
Magee, MS 39111
Term Expires: June 30, 2011

Jason Strong, Pharm.D.
Canton Discount
726 East Peace Street
Canton, MS 39046
Term Expires: June 30, 2011

Alvin Dixon, R.Ph.
182 Cherry Street
Clarksdale, MS 38614
Term expires: June 30, 2011

William Bastian, M.D.
Bastian Center of Pediatric
Endocrinology
1860 Chadwick Drive, Suite 206
Jackson, MS 39204
Term Expires: June 30, 2011

Upcoming Mississippi DUR Board Meeting Dates

February 19, 2009
May 21, 2009
August 20, 2009
November 19, 2009

DIVISION OF MEDICAID
OFFICE OF THE GOVERNOR
DRUG UTILIZATION REVIEW BOARD
AGENDA

November 20, 2008

Welcome	**Laura Gray, M.D.**
Old Business	**Laura Gray, M.D.**
Approval of Meeting Minutes	
Cost Management Analysis	**Ashleigh Holeman, Pharm.D.**
Pharmacy Program Update	**Paige Clayton, Pharm.D.**
New Business	**Ashleigh Holeman, Pharm.D.**
FDA Updates	
Atypical Antipsychotic Utilization in Children for ADHD/ODD	
Cost Savings Potential - Preventive Treatment of Migraine Headaches	
Duplicate Therapy with Sedative/Hypnotics	
Appropriate Use of Benzodiazepines	
Suboxone®/Subutex® Prior Authorization Process	
Other Criteria Recommendations	
Next Meeting Information	**Laura Gray, M.D.**

Mississippi Division of Medicaid
Drug Utilization Review (DUR) Board
Minutes of the September 25, 2008 Meeting

Members Attending: Laura Gray, M.D.; LeeVoulters, M.D.; Edgar Donahoe, M.D.; Mark Reed, M.D.; Lee Merritt, R.Ph.; Vickie Veazey, R.Ph.; Jason Strong, Pharm D.;
Members Absent: Roy Arnold, R.Ph.; William Bastian, M.D.; Alvin Dixon, R.Ph.; Frank Wade, M.D.; John Wallace, M.D.

Also Present:
DOM Staff: Judith Clark, R.Ph., DOM Pharmacy Bureau Director; Paige Clayton, Pharm.D. DOM DUR Coordinator; Carlis Faler, DOM Program Integrity Director
HID Staff: Ashleigh Holeman, Pharm.D., Project Manager; Kathleen Burns, R.N. Call Center Manager

Call to Order:
Laura Gray, Chairperson of the Board, called the meeting to order at 2:05 p.m.

Dr. Gray asked that the Board introduce themselves explaining that the Board was by majority new appointees by the Governor.

Judith Clark continued with an overview of the Board's objectives and appreciation from The Division of Medicaid for the Board's acceptance to serve the State in this capacity.

Old Business:
The Board was asked prior to the meeting to familiarize themselves with the sets of minutes and criteria in the packet, as they had previously been reviewed clinically by the Board at prior meetings but were not approved due to the lack of a quorum. It was noted that the Board would be asked to accept all previously reviewed minutes and criteria in one vote rather than reading through all the items individually. At this point, Dr. Gray asked for a motion to accept all prior minutes and criteria as directed earlier. Motion by Dr. Voulters; seconded by Dr. Reed. All voted in favor of the motion.

Cost Management Analysis:
Dr. Holeman began by presenting reports reflecting several months of data. Antipsychotic agents continued to lead the top 15 therapeutic classes by the total cost of claims for March 2008 through June 2008. The top drugs based on number of claims were led by hydrocodone-acetaminophen and followed by Amoxicillin. Dr. Clayton pointed out the far right column as the National rank and how these drugs in our state compare to the top 200 rank. Dr. Holeman continued with the top 25 drugs based on total claims cost by pointing to the leader, Risperdal®, followed by Synagis®, Singulair®, Prevacid® and lastly Feiba VH®.

Pharmacy Program Update:
Dr. Clayton presented an overview of the Annual DUR Report to CMS. She continued with clarification of HID as the Retrospective DUR Vendor and ACS as the ProDUR Vendor. The ProDUR report reflects the number of claims and the cost savings, which indicated several million dollars of cost savings. The Retrospective DUR report did not allow as much cost savings but still indicated around $600,000. Dr. Clayton offered a copy of this report to the Board as a mail-out and presented a copy for onsite viewing. Ms. Clark then presented a report on how claims from pharmacists interacted with the Medicaid system, and she noted that the promptness of the transaction is less than 0.4 seconds. She continued with education about the electronic PA offered between ACS and HID systems, which allows for a relief of paper work for the physician and his/her staff. Ms. Clark noted that Medicaid population changes have moved the pharmacy to interact with children more than adults, with the majority of the Mississippi Medicaid population being children.

FDA UPDATES:

Vivitrol (naltrexone)

8/12/2008: FDA informed healthcare professionals of the risk of adverse injection site reactions in patients receiving naltrexone. Naltrexone is indicated for the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiation of treatment. Naltrexone is administered as an intramuscular gluteal injection and should not be administered intravenously, subcutaneously, or inadvertently into fatty tissue. Physicians should instruct patients to monitor the injection site and contact them if they develop pain, swelling, tenderness, induration, bruising, pruritus, or redness at the injection site that does not improve or worsens within two weeks. Physicians should promptly refer patients with worsening injection site reactions to a surgeon. Read the FDA recommendations for healthcare professionals to consider regarding the use of Naltrexone injection.

Simvastatin Used With Amiodarone

8/08/2008: FDA notified healthcare professionals of the risk of muscle injury, rhabdomyolysis, which can lead to kidney failure or death, when simvastatin is used with amiodarone. This risk is dose-related and increases when a dose of simvastatin greater than 20 mg per day is given with amiodarone. Although a revision of the simvastatin labeling in 2002 described an increased risk of rhabdomyolysis when amiodarone is taken with simvastatin doses greater than 20 mg daily, FDA continues to receive reports of rhabdomyolysis in patients treated concurrently with amiodarone and simvastatin. Prescribers should be aware of the increased risk of rhabdomyolysis when simvastatin is prescribed with amiodarone, and they should avoid doses of simvastatin greater than 20 mg per day in patients taking amiodarone.

Erythropoiesis Stimulating Agents (ESAs) - Epoetin alfa (marketed as Procrit, Epogen), Darbepoetin alfa (marketed as Aranesp)

7/31/2008: FDA informed healthcare professionals of modifications to certain sections of the Boxed Warnings, Indications and Usage, and Dosage and Administration sections of prescribing information for Erythropoiesis Stimulating Agents (ESAs). The changes clarify the FDA-approved conditions for use of ESAs in patients with cancer and revise directions for dosing to state the hemoglobin level at which treatment with an ESA should be initiated. Additional revisions to prescribing information regarding ESAs use in patients receiving myelosuppressive therapy when the expected outcome is cure and when to initiate and discontinue ESA dosing will be forthcoming. FDA continues to encourage healthcare professionals to discuss with their patients before starting or continuing therapy with ESAs, the benefits of treatment with ESAs and the potential and demonstrated risks of ESAs for thrombovascular events, shortened time to tumor progression or recurrence, and shortened survival time.

Mitoxantrone Hydrochloride (marketed as Novantrone and generics)

7/29/2008: FDA reminded health care professionals who treat patients with mitoxantrone about recommendations that left ventricular ejection fraction (LVEF) be evaluated before initiating treatment and prior to administering each dose of mitoxantrone. FDA offered additional recommendations for cardiac monitoring to detect late-occurring cardiac toxicity, and provided information for patients with multiple sclerosis who receive the drug.

These recommendations were established in 2005 in response to post-marketing reports and case reports in the medical literature that described decreases in LVEF or frank congestive heart failure in patients with MS who had received cumulative doses of mitoxantrone that were lower than 100 mg/m^2. Since that time, FDA has received information from a post-marketing safety study that demonstrated there is poor adherence to these recommendations in clinical practice. FDA is working with the manufacturers to educate healthcare providers to adhere to cardiac monitoring recommendations for patients with MS.

Abacavir (marketed as Ziagen) and Abacavir-containing Medications

7/24/2008] FDA informed healthcare professionals that serious and sometimes fatal hypersensitivity reactions (HSR) caused by abacavir therapy are significantly more common in patients with a particular human leukocyte antigen (HLA) allele, HLA-B*5701. FDA reviewed data from two studies that support a recommendation for pre-therapy screening for the presence of the HLA-B*5701 allele and the selection of alternative therapy in positive subjects. Genetic tests for HLA-B*5701 are available and all patients should be screened for the HLA-B*5701 allele before starting or restarting treatment with abacavir or abacavir-containing medications.

Development of clinically suspected abacavir HSR requires immediate and permanent discontinuation of abacavir therapy in all patients, including patients negative for HLA-B*5701.

Sodium Polystyrene Sulfonate Suspension

7/16/2008: Roxane Laboratories, Inc. informed healthcare professionals of the recall of two lots of Sodium Polystyrene Sulfonate Suspension, USP, 15 g/60 mL Unit dose bottles (NDC 0054-0165-51; lot 856396A Exp April 2010, and lot 856693A Exp May 2010), a product used to treat hyperkalemia. A sample of one of the affected lots tested positive for a strain of yeast, which could potentially affect immunocompromised patients. Symptoms of a yeast infection range from thrush, skin rash, and blood infections. If patients develop an infection they should consult their physician. Pharmacists should determine if any of the referenced product has been dispensed and retrieve it. Additionally, pharmacists and wholesalers of the product should discontinue distribution and use of the referenced lots immediately and contact the manufacturer regarding returning the product.

Avastin (bevacizumab)

7/14/2008: Genentech, Inc. informed healthcare professionals of reports of several cases of microangiopathic hemolytic anemia (MAHA) in patients with solid tumors receiving Avastin in combination with sunitinib malate. Avastin is not approved for use in combination with sunitinib malate and this combination is not recommended. Twenty-five patients were enrolled in a Phase I dose-escalation study combining Avastin and sunitinib malate. The study consisted of 3 cohorts using a fixed dose of Avastin at 10mg/kg/IV every 2 weeks and escalating doses of sunitinib that included 25, 37.5, and 50 mg orally daily given in a 4 weeks on/ 2 weeks off schedule. Five of 12 patients at the highest sunitinib dose level exhibited laboratory findings consistent with MAHA. Two of these cases were considered severe with evidence of thrombocytopenia, anemia, reticulocytosis, reductions in serum haptoglobin, schistocytes on peripheral smear, modest increases in serum creatinine levels, and severe hypertension, reversible posterior leukoencephalopathy syndrome, and proteinuria. The findings in these two cases were reversible within three weeks upon discontinuation of both drugs without additional interventions. Healthcare professionals should report cases of MAHA or any serious adverse events suspected to be associated with the use of Avastin.

Fluoroquinolone Antimicrobial Drugs

7/08/2008: FDA notified healthcare professionals that a BOXED WARNING and Medication Guide are to be added to the prescribing information to strengthen existing warnings about the increased risk of developing tendinitis and tendon rupture in patients taking fluoroquinolones for systemic use.

Fluoroquinolones are associated with an increased risk of tendinitis and tendon rupture. This risk is further increased in those over age 60, in kidney, heart, and lung transplant recipients, and with use of concomitant steroid therapy. Physicians should advise patients, at the first sign of tendon pain, swelling, or inflammation, to stop taking the fluoroquinolone, to avoid exercise and use of the affected area, and to promptly contact their doctor about changing to a non-fluoroquinolone antimicrobial drug. Selection of a fluoroquinolone for the treatment or prevention of an infection should be limited to those conditions that are proven or strongly suspected to be caused by bacteria.

Antipsychotics, Conventional and Atypical

6/16/2008: FDA notified healthcare professionals that both conventional and atypical antipsychotics are associated with an increased risk of mortality in elderly patients treated for dementia-related psychosis. In April 2005, FDA notified healthcare professionals that patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death. Since issuing that notification, FDA has reviewed additional information that indicates the risk is also associated with conventional antipsychotics. Antipsychotics are not indicated for the treatment of dementia-related psychosis. The prescribing information for all antipsychotic drugs will now include the same information about this risk in a BOXED WARNING and the WARNINGS section.

Tumor Necrosis Factor (TNF) Blockers (marketed as Remicade, Enbrel, Humira, and Cimzia)

6/03/2008: FDA issued an Early Communication About an Ongoing Safety Review to inform healthcare professionals that the Agency is investigating a possible association between the use of Tumor Necrosis Factor (TNF) blockers and the development of lymphoma and other cancers in

children and young adults. FDA is investigating approximately 30 reports of cancer in children and young adults. These reports were submitted to FDA's Adverse Event Reporting System over a ten-year interval, beginning in 1998 through April 29, 2008. These reports describe cancer occurring in children and young adults who began taking TNF blockers (along with other immunosuppressive medicines such as methotrexate, azathioprine or 6-mercaptopurine), when they were ages 18 or less, to treat juvenile idiopathic arthritis, Crohn's disease or other diseases. Approximately half of the cancers were lymphomas, including both Hodgkin's and non-Hodgkin's lymphoma. Long-term studies are necessary to provide definitive answers about whether TNF blockers increase the occurrence of cancers in children because cancers may take a long time to develop and may not be detected in short-term studies. Until the evaluation is completed, healthcare providers, parents, and caregivers should be aware of the possible risk of lymphoma and other cancers in children and young adults when deciding how to best treat these patients.

Mycophenolate Mofetil [MMF] (marketed as CellCept)
Mycophenolic Acid [MPA] (marketed as Myfortic)
Inosine Monophosphate Dehydrogenase Inhibitors (IMPDH) Immunosuppressants

5/16/2008: FDA is aware of reports of infants born with serious congenital anomalies, including microtia and cleft lip and palate, following exposure to mycophenolate mofetil (MMF) during pregnancy. MMF, the active drug substance in CellCept, is an ester of the active metabolite mycophenolic acid (MPA), the active drug substance in Myfortic. In most cases, the mothers were taking MMF following an organ transplant to prevent organ rejection. However, some mothers taking MMF were being treated for immune-mediated conditions such as systemic lupus erythematosus (SLE) and erythema multiforme. Treatment began before their pregnancies and continued into the first trimester or until the pregnancy was detected. MMF and MPA increase the risk of spontaneous abortion in the first trimester and can cause congenital malformations in the offspring of women who are treated during pregnancy.

FDA is continuing to work with the manufacturers of these drug products to develop and implement means to mitigate the risks of fetal exposure. See the FDA Healthcare Professional Information Sheet containing considerations and recommendations for clinicians prior to prescribing MMF or MPA to women of childbearing potential.

Enbrel (etanercept)

5/01/2008: Amgen and Wyeth Pharmaceuticals informed healthcare professionals of revisions to prescribing information for Enbrel. The revisions include a BOXED WARNING about infections, including serious infections leading to hospitalization or death that have been observed in patients treated with Enbrel. Infections have included bacterial sepsis and tuberculosis. The ADVERSE REACTIONS section of the label was updated to include information regarding global clinical studies and the rate of occurrence of tuberculosis in patients treated with Enbrel. Healthcare professionals should screen patients for latent tuberculosis infection before beginning Enbrel. Patients should be educated about the symptoms of infection and closely monitored for signs and symptoms of infection during and after treatment with the drug. Patients who develop an infection should be evaluated for appropriate antimicrobial treatment and, in patients who develop a serious infection, Enbrel should be discontinued.

Regranex (becaplermin) Gel

6/06/2008: FDA informed healthcare professionals that a Boxed Warning was added to prescribing information for Regranex that describes an increased risk of death from cancer in patients treated with three or more tubes of Regranex compared with those patients who did not use the product. FDA recommends that Regranex be used only when the benefits can be expected to outweigh the risks.

DUR OVERVIEW:

Dr. Holeman discussed the overview of the DUR intervention process with the Board members to enlighten the new members and as a review for the other members.

OFF-LABEL USE OF ATYPICAL ANTIPSYCHOTICS FOR CHILDREN WITH ADHD AND/OR ODD:

Dr. Holeman presented a report resulting from the increased PA requests HID receives daily for atypical antipsychotics being used in pediatric patients with the only diagnoses provided being ADHD or ODD,

neither of which are FDA-approved indications for medications in this class. This has raised concerns about the increased use of atypical antipsychotics in children and the future medical conditions that might arise from this off-label use. HID conducted an analysis of claims for children under 18 with medical claims indicating the diagnoses of ADHD and ODD only. It was found that the largest number of beneficiaries receiving atypical antipsychotics were between 13 and 16 years of age. There was also a substantial use of atypical antipsychotics in children as young as six with these diagnoses.
Recommendation: HID recommends a retrospective DUR criterion to identify these pediatric patients with ADHD and/or ODD who have received one or more atypical antipsychotics and do not have an FDA-approved diagnosis. Motion: Dr. Gray Seconded: Dr. Voulters; All voted in favor of motion.

GENERALIZED ANXIETY DISORDER (GAD):
Antidepressants are the preferred class for the treatment of GAD, with the selective SSRIs being the first-line agents. Lexapro® and paroxetine immediate-release are the only SSRIs with specific indications for GAD, although most treatment guidelines recommend treatment with any of the SSRIs. Benzodiazepines do have a role in the treatment of GAD, but treatment guidelines recommend that their use be short-term, not to exceed 2-4 weeks.
Recommendations: HID recommends distribution of a Medicaid Prescribing Update or "one-pager" that provides a description of this disorder and, more importantly, proper treatment recommendations for GAD based on treatment guidelines. This would be distributed by the Academic Detailers to the prescribers and as well as available by a link from the Division of Medicaid website. Motion: Dr. Reed; Seconded: Dr Voulters; all voted in favor of motion.

CARISOPRODOL UTILIZATION UPDATE:
Based on directives from the DUR Board and the P & T Committee, the Division of Medicaid began requiring prior authorization on carisoprodol-containing products beginning on July 1, 2008. HID generated a report illustrating the periods leading up to and following the implementation of the PA for these products.
Based on the information submitted to the Board, the prior authorization process was a success in reducing overall utilization of carisoprodol as well as the number of beneficiaries receiving multiple prescriptions for these products. The total cost to the Division of Medicaid was significantly reduced. Compared to the months leading up to the PA implementation, the cost to DOM for carisoprodol-containing products decreased by nearly 98% in July 2008. It is evident that the Division of Medicaid took the proper steps in reigning in potential misuse of carisoprodol products at the expense of the state.

IMPORTANT ISSUES SURROUNDING SUBOXONE/SUBUTEX®:
Dr. Holeman presented an extensive report on Suboxone® and Subutex®, beginning by explaining that these are pharmacological agents designed to aid in the treatment of opioid dependence. Concern has been provoked among the HID Clinical Staff members based on prior authorization requests received for these two products. Many times these requests are for doses outside the recommended ranges set forth by the manufacturer, especially for first-time users of these agents. Considering that Suboxone® and Subutex® are used for the treatment of opioid dependence, concurrent use with opioid analgesics is a troubling issue. The Division of Medicaid spent roughly $13,000 in April 2008 alone on Suboxone® or Subutex® therapy that was not utilized in the appropriate manner by these beneficiaries. Of the 164 Mississippi Medicaid beneficiaries who received these medications in April 2008, 41 of these beneficiaries also received at least one prescription for a benzodiazepine. 10 of these same beneficiaries received 2 or more prescriptions for a benzodiazepine along with these products. It was noted that these agents allow for office-based treatment of drug addiction, thereby increasing treatment retention rates and patient freedom to continue the normal activities of daily living. However, data provided has proven, especially in the unsupervised residential setting, that there is potential for misuse of these products. The Division of Medicaid has placed quantity limits on opioid products of 62 tablets per every rolling 31 days. Currently, these quantity limits are not cumulative across all preparations of opioids. HID and The Division of Medicaid asked for a directive from the DUR Board in order to place cumulative limits of 62 tablets per every 31 days. Dr. Donahoe suggested that there be an exception made with this limit for the treatment of cancer and severe arthritis patients. It was noted that a physician may submit a Maximum Unit Override PA form to obtain additional medications for this critical group of patients. Motion: Dr. Gray; Seconded: Dr. Donahoe; All voted in favor of this motion.

GROWTH SUPPRESSION AND ADHD TREATMENTS:
A recent observation was made in the HID Call Center concerning some patients receiving growth hormones. It was noted that several children requiring prior authorization for growth hormones were also receiving ADHD agents as well. The question was raised whether the medications used to treat ADHD were the cause of the growth suppression in these patients, who were now requiring treatment with synthetic growth hormones. A Clinical study was done by the HID staff to determine if this might be a possibility. As a result, HID gathered utilization data for both therapeutic classes which indicated that the number of patients identified receiving both treatments was not overwhelming. Dr. Voulters provided information that many studies have been done and much data reviewed revealing that there is no correlation between ADHD medications and the growth suppression of patients requiring treatments with synthetic growth hormones. Therefore no criteria were recommended to further the study of this issue.

ASTHMA:
Based on a directive from DOM, HID developed a Medicaid Prescribing Update to highlight the updated treatment recommendations found within the new EPR3 Guidelines. This Update coordinated with the implementation of a new preferred drug lists that included changes to the respiratory agents beginning July 1, 2008. HID began the distribution of this document to prescribers by the Academic Detailing staff and made it available by a link from the Division of Medicaid website. Dr. Donahoe stated that by the end of 2008, generic albuterol inhalers will be obsolete and this will put a hardship on patients when considering the brand medication limits for adult Medicaid beneficiaries. He requested that DOM might make a carve-out for these medications as this was critical to the care of his severe asthma patients in the Delta. Ms. Clark was requested to take this to a higher authority for guidance on this sensitive issue. She agreed to do this immediately and would report back at possibly the next DUR Board meeting with the outcome of this request.

SYNAGIS®:
Dr. Holeman reviewed the implementation of the new 2008-2009 criteria and PA process for Synagis®. She noted a new statement added to the prior authorization form that the physician must sign stating that he acknowledges that he is responsible for the medication being given to the patient it is designated for and should that not be possible, then he would notify the specialty pharmacy immediately. The Division of Medicaid loses many thousands of dollars every year by medications being allowed to remain in the physician's refrigerators without Medicaid being credited back for this spent money. It is the intention of Medicaid to trim this waste in the upcoming season by asking the physicians to be responsible for the tracking of the spent dollars and reimbursement of dollars for unused Synagis®. It is also the intent that every beneficiary who qualifies for treatment with this medication will receive it without any delays. It is also encouraged that if Medicaid pays for a medication that it is given to the child it was intended for.

OTHER CRITERIA RECOMMENDATIONS:
Dr. Holeman reviewed the remaining 3 criteria that were left for approving. Motion: Dr. Voulters; Seconded: Ms Veazey; all voted in favor of the recommendations.

Dr. Gray reminded the Board of the next meeting on November 20, 2008 and asked for a motion that the meeting would be adjourned at 3:15 p.m. Motion: Dr. Voulters; Seconded: Dr. Reed

Respectfully Submitted:
Health Information Designs, Inc.

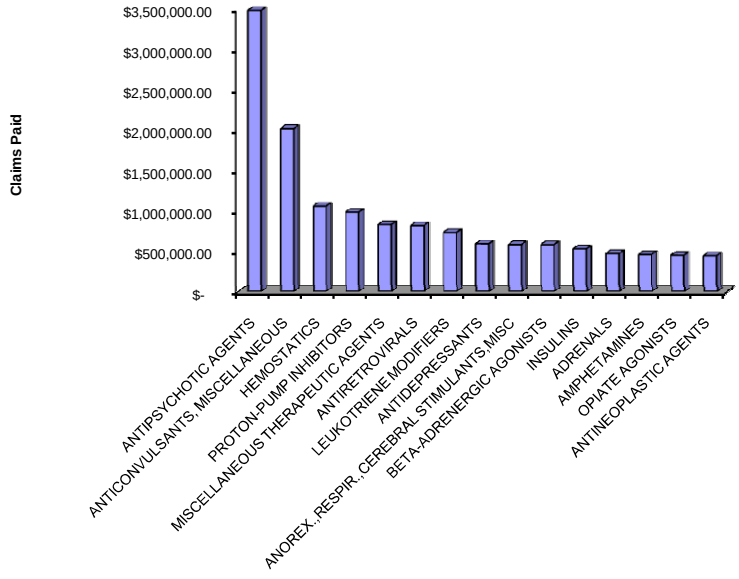
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 07/01/08-07/31/08

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	10,741	$ 3,483,707.60	$ 324.34	3.10%
ANTICONVULSANTS, MISCELLANEOUS	11,673	$ 2,018,154.92	$ 172.89	3.37%
HEMOSTATICS	53	$ 1,053,754.30	$19,882.16	0.02%
PROTON-PUMP INHIBITORS	6,478	$ 980,130.61	$ 151.30	1.87%
MISCELLANEOUS THERAPEUTIC AGENTS	2,479	$ 828,041.24	$ 334.02	0.71%
ANTIRETROVIRALS	1,128	$ 814,643.92	$ 722.20	0.33%
LEUKOTRIENE MODIFIERS	6,711	$ 726,093.85	$ 108.19	1.93%
ANTIDEPRESSANTS	13,877	$ 588,668.82	$ 42.42	4.00%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	4,562	$ 577,811.79	$ 126.66	1.32%
BETA-ADRENERGIC AGONISTS	9,238	$ 576,353.06	$ 62.39	2.66%
INSULINS	3,696	$ 525,577.43	$ 142.20	1.07%
ADRENALS	6,836	$ 467,688.09	$ 68.42	1.97%
AMPHETAMINES	3,652	$ 454,407.44	$ 124.43	1.05%
OPIATE AGONISTS	26,994	$ 446,206.30	$ 16.53	7.78%
ANTINEOPLASTIC AGENTS	902	$ 439,866.59	$ 487.66	0.26%
TOTAL TOP 15	109,020	$ 13,981,105.96	$ 128.24	31.43%

Total Rx Claims	346,829
From 07/01/08-07/31/08	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



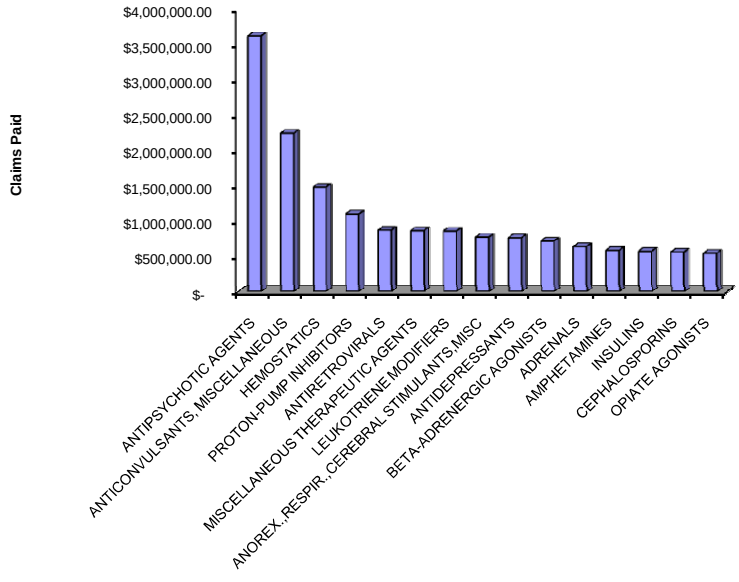
MISSISSIPPI MEDICAID
Cost Management Analysis

TOP 15 THERAPEUTIC CLASSES BY TOTAL COST OF CLAIMS FROM 08/01/08-08/31/08

AHFS Therapeutic Class	Rx	Paid	Paid/Rx	% Total Claims
ANTIPSYCHOTIC AGENTS	11,207	$ 3,623,058.40	$ 323.29	2.92%
ANTICONVULSANTS, MISCELLANEOUS	12,378	$ 2,242,103.30	$ 181.14	3.23%
HEMOSTATICS	59	$ 1,475,213.77	$25,003.62	0.02%
PROTON-PUMP INHIBITORS	7,118	$ 1,093,638.26	$ 153.64	1.86%
ANTIRETROVIRALS	1,156	$ 867,176.69	$ 750.15	0.30%
MISCELLANEOUS THERAPEUTIC AGENTS	2,542	$ 857,768.32	$ 337.44	0.66%
LEUKOTRIENE MODIFIERS	7,870	$ 851,713.48	$ 108.22	2.05%
ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	6,054	$ 766,280.02	$ 126.57	1.58%
ANTIDEPRESSANTS	14,779	$ 755,734.74	$ 51.14	3.86%
BETA-ADRENERGIC AGONISTS	12,059	$ 710,777.16	$ 58.94	3.15%
ADRENALS	8,666	$ 633,196.18	$ 73.07	2.26%
AMPHETAMINES	4,466	$ 578,939.87	$ 129.63	1.17%
INSULINS	3,930	$ 565,721.54	$ 143.95	1.03%
CEPHALOSPORINS	10,410	$ 555,445.26	$ 53.36	2.72%
OPIATE AGONISTS	27,701	$ 538,618.97	$ 19.44	7.23%
TOTAL TOP 15	130,395	$ 16,115,385.96	$ 123.59	34.02%

Total Rx Claims	383,281
From 08/01/08-08/31/08	

Top 15 Therapeutic Classes
Based on Total Cost of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

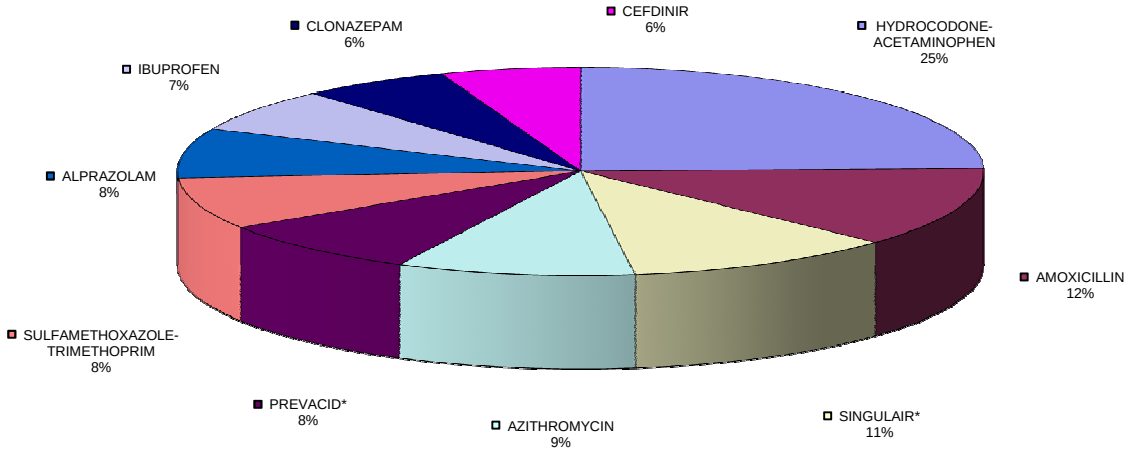
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 07/01/08-07/31/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	15,212	$ 129,582.53	1
AMOXICILLIN	PENICILLINS	7,659	$ 66,836.78	3
SINGULAIR*	LEUKOTRIENE MODIFIERS	6,706	$ 725,439.98	2
AZITHROMYCIN	MACROLIDES	5,891	$ 189,071.39	6
PREVACID*	PROTON-PUMP INHIBITORS	5,281	$ 842,990.67	8
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	4,974	$ 50,224.47	62
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,756	$ 34,578.99	9
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	4,188	$ 30,735.73	14
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,689	$ 48,833.27	25
CEFDINIR	CEPHALOSPORINS	3,469	$ 248,907.81	105
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	3,246	$ 147,337.08	26
ACETAMINOPHEN-CODEINE	OPIATE AGONISTS	3,223	$ 23,305.18	41
FERROUS SULFATE	IRON PREPARATIONS	3,127	$ 11,064.75	113
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	3,065	$ 80,196.83	67
CETIRIZINE HCL	SECOND GENERATION ANTIHISTAMINES	3,008	$ 58,707.51	~
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	3,005	$ 53,292.28	23
CEPHALEXIN	CEPHALOSPORINS	2,980	$ 40,646.64	18
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	2,917	$ 88,889.56	108
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	2,596	$ 29,739.18	55
AMLODIPINE BESYLATE	DIHYDROPYRIDINES	2,548	$ 64,985.42	15
RANITIDINE HCL	HISTAMINE H2-ANTAGONISTS	2,517	$ 69,258.81	47
ADDERALL XR*	AMPHETAMINES	2,509	$ 379,415.87	36
LISINOPRIL	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS	2,469	$ 30,981.56	2
ALBUTEROL	BETA-ADRENERGIC AGONISTS	2,434	$ 61,365.71	27
CITALOPRAM HBR	ANTIDEPRESSANTS	2,341	$ 19,744.82	35
TOTAL TOP 25		103,810	$ 3,526,132.82	

Total Rx Claims From 07/01/08-07/31/08	346,829

* Indicates preferred products on the Preferred Drug List

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

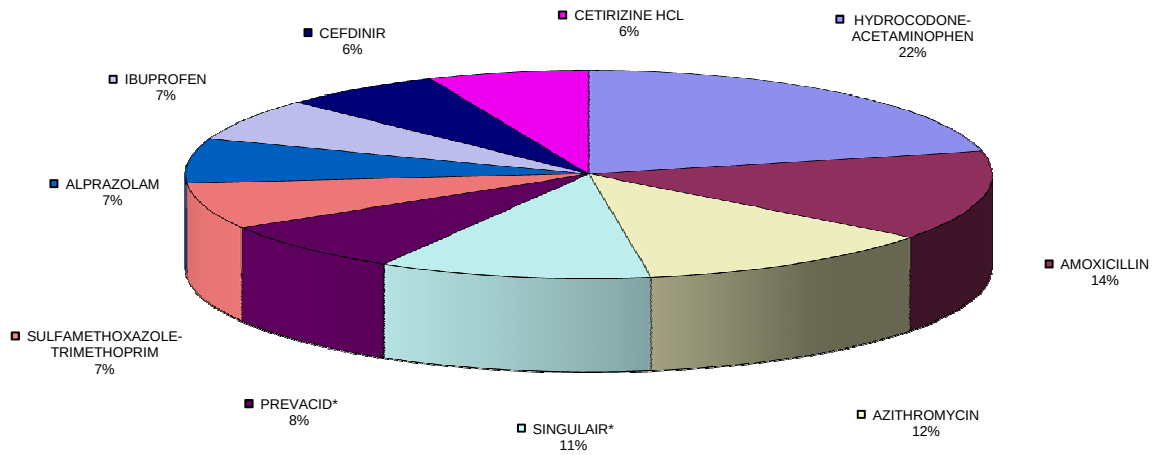
TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 08/01/08-08/31/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
HYDROCODONE-ACETAMINOPHEN	OPIATE AGONISTS	15,459	$ 163,342.51	1
AMOXICILLIN	PENICILLINS	10,037	$ 92,980.91	3
AZITHROMYCIN	MACROLIDES	8,766	$ 311,904.34	6
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,864	$ 850,954.64	2
PREVACID*	PROTON-PUMP INHIBITORS	5,724	$ 919,814.54	8
SULFAMETHOXAZOLE-TRIMETHOPRIM	SULFONAMIDES (SYSTEMIC)	5,231	$ 61,549.91	62
ALPRAZOLAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	4,953	$ 41,272.22	9
IBUPROFEN	NONSTEROIDAL ANTI-INFLAMMATORY AGENTS	4,764	$ 36,694.54	14
CEFDINIR	CEPHALOSPORINS	4,641	$ 345,578.11	105
CETIRIZINE HCL	SECOND GENERATION ANTIHISTAMINES	4,637	$ 86,731.74	~
ALBUTEROL SULFATE	BETA-ADRENERGIC AGONISTS	4,307	$ 126,834.78	67
AMOX TR-POTASSIUM CLAVULANATE	PENICILLINS	4,205	$ 223,745.19	26
ED A-HIST	PROPYLAMINE DERIVATIVES	3,924	$ 34,671.28	~
CLONAZEPAM	BENZODIAZEPINES (ANTICONVULSANTS)	3,816	$ 71,663.68	25
CEPHALEXIN	CEPHALOSPORINS	3,315	$ 50,779.64	18
ACETAMINOPHEN-CODEINE	OPIATE AGONISTS	3,257	$ 26,077.51	41
ADDERALL XR*	AMPHETAMINES	3,166	$ 480,573.72	36
ALBUTEROL	BETA-ADRENERGIC AGONISTS	3,144	$ 73,829.94	27
LORAZEPAM	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)	3,107	$ 82,107.16	23
FERROUS SULFATE	IRON PREPARATIONS	3,106	$ 10,978.12	113
PROMETHAZINE HCL	PHENOTHIAZINE DERIVATIVES	2,934	$ 35,608.08	55
MUPIROCIN	ANTIBACTERIALS (SKIN & MUCOUS MEMBRANE)	2,827	$ 106,637.40	108
RISPERIDONE	ANTIPSYCHOTIC AGENTS	2,729	$ 685,106.29	~
AMLODIPINE BESYLATE	DIHYDROPYRIDINES	2,718	$ 121,424.43	15
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,679	$ 369,955.41	44
TOTAL TOP 25		121,310	$ 5,410,816.09	

Total Rx Claims From 08/01/08-08/31/08	383,281

* Indicates preferred products on the Preferred Drug List

Top 10 Drugs
Based on Number of Claims



MISSISSIPPI MEDICAID
Cost Management Analysis

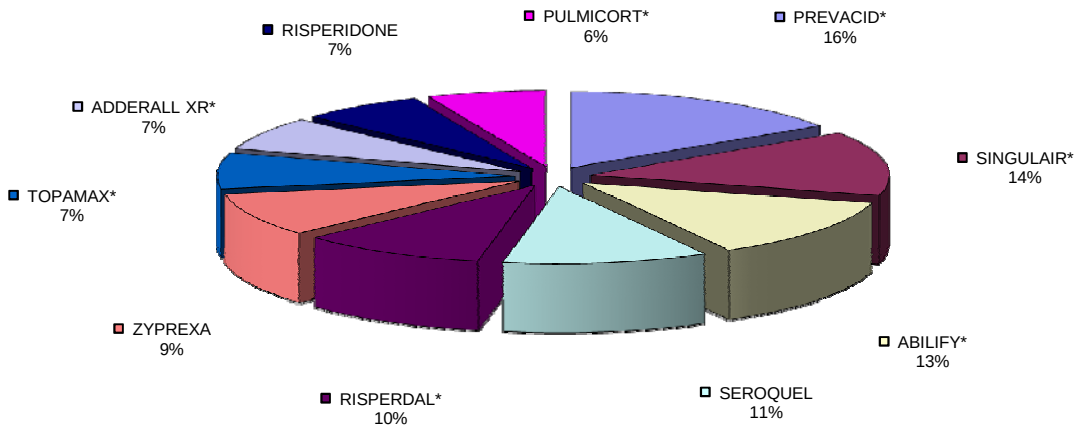
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 07/01/08-07/31/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
PREVACID*	PROTON-PUMP INHIBITORS	5,281	$ 842,990.67	4
SINGULAIR*	LEUKOTRIENE MODIFIERS	6,706	$ 725,439.98	6
ABILIFY*	ANTIPSYCHOTIC AGENTS	1,469	$ 679,786.05	15
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,662	$ 595,799.96	7
RISPERDAL*	ANTIPSYCHOTIC AGENTS	1,850	$ 542,963.73	14
ZYPREXA	ANTIPSYCHOTIC AGENTS	916	$ 490,684.59	18
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,332	$ 402,759.05	13
ADDERALL XR*	AMPHETAMINES	2,509	$ 379,415.87	27
RISPERIDONE	ANTIPSYCHOTIC AGENTS	1,517	$ 359,793.55	~
PULMICORT*	ADRENALS	1,239	$ 342,948.32	64
GEODON*	ANTIPSYCHOTIC AGENTS	890	$ 326,975.65	58
FEIBA VH IMMUNO	HEMOSTATICS	7	$ 325,688.99	~
LAMICTAL*	ANTICONVULSANTS, MISCELLANEOUS	878	$ 283,565.40	17
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	997	$ 279,748.38	57
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,478	$ 278,894.84	3
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,025	$ 278,490.41	34
CEFDINIR	CEPHALOSPORINS	3,469	$ 248,907.81	31
ADVATE	HEMOSTATICS	6	$ 240,838.21	~
DEPAKOTE*	ANTICONVULSANTS, MISCELLANEOUS	963	$ 207,856.22	67
EFFEXOR XR*	ANTIDEPRESSANTS	1,206	$ 201,514.98	8
RISPERDAL CONSTA	ANTIPSYCHOTIC AGENTS	259	$ 198,940.78	160
PLAVIX*	PLATELET-AGGREGATION INHIBITORS	1,434	$ 193,277.86	5
LIPITOR*	HMG-COA REDUCTASE INHIBITORS	1,762	$ 190,472.48	1
AZITHROMYCIN	MACROLIDES	5,891	$ 189,071.39	2
DEPAKOTE ER*	ANTICONVULSANTS, MISCELLANEOUS	1,016	$ 186,696.34	66
TOTAL TOP 25		46,762	$ 8,993,521.51	

Total Rx Claims From 07/01/08-07/31/08	346,829

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



MISSISSIPPI MEDICAID
Cost Management Analysis

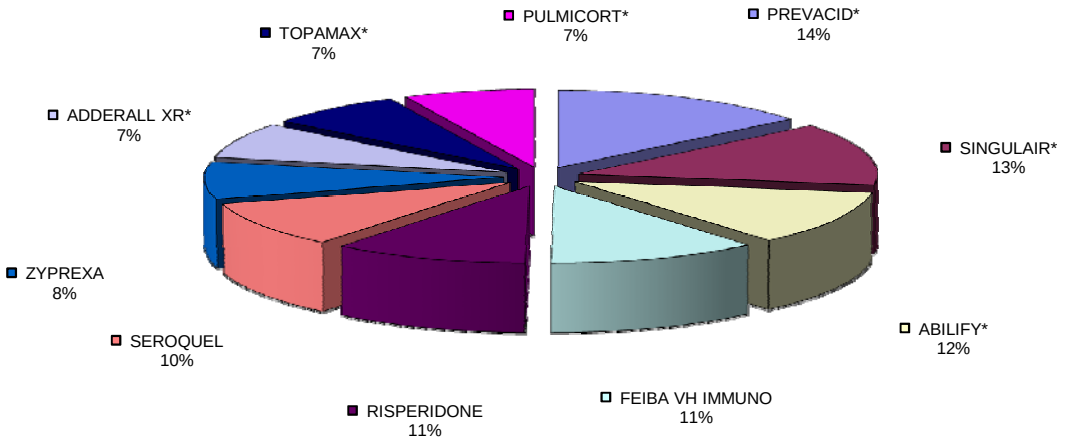
TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 08/01/08-08/31/08

Drug	AHFS Therapeutic Class	Rx	Paid	Top 200 Rank
PREVACID*	PROTON-PUMP INHIBITORS	5,724	$ 919,814.54	4
SINGULAIR*	LEUKOTRIENE MODIFIERS	7,864	$ 850,954.64	6
ABILIFY*	ANTIPSYCHOTIC AGENTS	1,637	$ 750,158.48	15
FEIBA VH IMMUNO	HEMOSTATICS	8	$ 738,684.13	~
RISPERIDONE	ANTIPSYCHOTIC AGENTS	2,729	$ 685,106.29	~
SEROQUEL	ANTIPSYCHOTIC AGENTS	1,715	$ 624,152.44	7
ZYPREXA	ANTIPSYCHOTIC AGENTS	892	$ 507,466.01	18
ADDERALL XR*	AMPHETAMINES	3,166	$ 480,573.72	27
TOPAMAX*	ANTICONVULSANTS, MISCELLANEOUS	1,474	$ 476,493.17	13
PULMICORT*	ADRENALS	1,639	$ 458,459.68	64
CONCERTA*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	2,679	$ 369,955.41	34
CEFDINIR	CEPHALOSPORINS	4,641	$ 345,578.11	31
GEODON*	ANTIPSYCHOTIC AGENTS	928	$ 332,810.25	58
ADVAIR DISKUS*	BETA-ADRENERGIC AGONISTS	1,634	$ 317,242.79	3
AZITHROMYCIN	MACROLIDES	8,766	$ 311,904.34	2
KEPPRA*	ANTICONVULSANTS, MISCELLANEOUS	1,110	$ 308,468.37	57
RISPERDAL*	ANTIPSYCHOTIC AGENTS	853	$ 240,266.93	14
GABAPENTIN	ANTICONVULSANTS, MISCELLANEOUS	2,116	$ 228,538.77	11
AMOX TR-POTASSIUM CL	PENICILLINS	4,205	$ 223,745.19	9
EFFEXOR XR*	ANTIDEPRESSANTS	1,314	$ 215,127.26	8
PLAVIX*	PLATELET-AGGREGATION INHIBITORS	1,581	$ 213,836.23	5
FOCALIN XR*	ANOREX.,RESPIR.,CEREBRAL STIMULANTS,MISC	1,617	$ 204,359.39	133
LIPITOR*	HMG-COA REDUCTASE INHIBITORS	1,869	$ 202,638.77	1
STRATTERA*	CENTRAL NERVOUS SYSTEM AGENTS, MISC.	1,289	$ 198,994.32	73
DEPAKOTE ER*	ANTICONVULSANTS, MISCELLANEOUS	1,048	$ 188,444.70	66
TOTAL TOP 25		62,498	$ 10,393,773.93	

Total Rx Claims From 08/01/08-08/31/08	383,281

** Indicates preferred products on the Preferred Drug List*

Top 10 Drugs
Based on Total Claims Cost



FDA Updates

The following information is provided to the DUR Board to assist in identifying drug products with potential for concern surrounding safety and appropriate utilization. Most of the safety alert information provided is derived from recent FDA safety alerts. While many of the alerts included are not Black Box Warning additions or updates, they are labeling changes or updates with relevance worthy of action by FDA.

Included for reference, the following is the Code of Federal Regulations definition for Black Box Warnings. (Citation: Title 21 CFR 201.57 Section E)

(e) Warnings. Under this section heading, the labeling shall describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and steps that should be taken if they occur. The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved. A specific warning relating to a use not provided for under the "Indications and Usage: section of labeling may be required by the Food and Drug Administration if the drug is commonly prescribed for a disease of condition, and there is lack of substantial evidence of effectiveness for that disease or condition, and such usage is associated with serious risk or hazard. Special problems, particularly those that may lead to death or serious risk or hazard. Special problems, particularly those that may lead to death or serious injury, may be required by the Food and Drug Administration to be placed in a prominently displayed box. The boxed warning ordinarily shall be based on clinical data, but serious animal toxicity may also be the basis of a boxed warning in the absence of clinical data. If a boxed warning is required, its location will be specified by the Food and Drug Administration. The frequency of these adverse reactions and, if known, the approximate mortality and morbidity rates for patients sustaining the reaction, which are important to safe and effective used of the drug, shall be expressed as provided under the "Adverse Reactions" section of the labeling.

Tumor necrosis factor-alpha blockers (TNF blockers), Cimzia (certolizumab pegol), Enbrel (etanercept), Humira (adalimumab), and Remicade (infliximab)
FDA notified healthcare professionals that pulmonary and disseminated histoplasmosis, coccidioidomycosis, blastomycosis and other opportunistic infections are not consistently recognized in patients taking tumor necrosis factor-α blockers (TNF blockers). This has resulted in delays in appropriate treatment, sometimes resulting in death. For patients taking TNF blockers who present with signs and symptoms of possible systemic fungal infection, such as fever, malaise, weight loss, sweats, cough, dypsnea, and/or pulmonary infiltrates, or other serious systemic illness with or without concomitant shock, healthcare professionals should ascertain if patients live in or have traveled to areas of endemic mycoses. For patients at risk of histoplasmosis and other invasive fungal infections, clinicians should consider empiric antifungal treatment until the pathogen(s) are identified.

Rituxan (rituximab) Injection
Genentech informed healthcare professionals of revisions to prescribing information for Rituxan regarding a case of progressive multifocal leukoencephalopathy (PML) leading to death in a patient with

rheumatoid arthritis who received Rituxan in a long-term safety extension clinical study. The patient developed a JC virus infection with resultant PML and death 18 months after taking the last dose of Rituxan. Healthcare professionals treating patients with Rituxan should consider PML in any patient presenting with new onset neurologic manifestations. Additionally, consultation with a neurologist, brain MRI and lumbar puncture should be considered as clinically indicated.

Tarceva (erlotinib) Tablets

OSI and Genentech notified healthcare professionals that cases of hepatic failure and hepatorenal syndrome, including fatalities, have been reported during use of Tarceva, particularly in patients with baseline hepatic impairment. Patients with hepatic impairment receiving Tarceva should be closely monitored during therapy and the product should be used with extra caution in patients with total bilirubin >3x ULN. Dosing should be interrupted or discontinued if changes in liver function are severe, such as doubling of total bilirubin and/or tripling of transaminases in the setting of pretreatment values outside the normal range. New information from a pharmacokinetic study in patients with moderate hepatic impairment associated with significant liver tumor burden has been provided in the revised prescribing information, and other recommendations are included in the WARNINGS and DOSAGE AND ADMINISTRATION sections.

Statin drugs and amyotrophic lateral sclerosis (ALS)

An FDA analysis provides new evidence that the use of statins does not increase incidence of amyotrophic lateral sclerosis (ALS), a neurodegenerative disease often referred to as "Lou Gehrig's Disease." The FDA analysis, undertaken after the agency received a higher than expected number of reports of ALS in patients on statins, is based on data from 41 long-term controlled clinical trials. The results showed no increased incidence of the disease in patients treated with a statin compared with placebo.

The FDA is anticipating the completion of a case-control or epidemiological study of ALS and statin use. Results from this study should be available within 6-9 months. FDA is also examining the feasibility of conducting additional epidemiologic studies to examine the incidence and clinical course of ALS in patients taking statins.

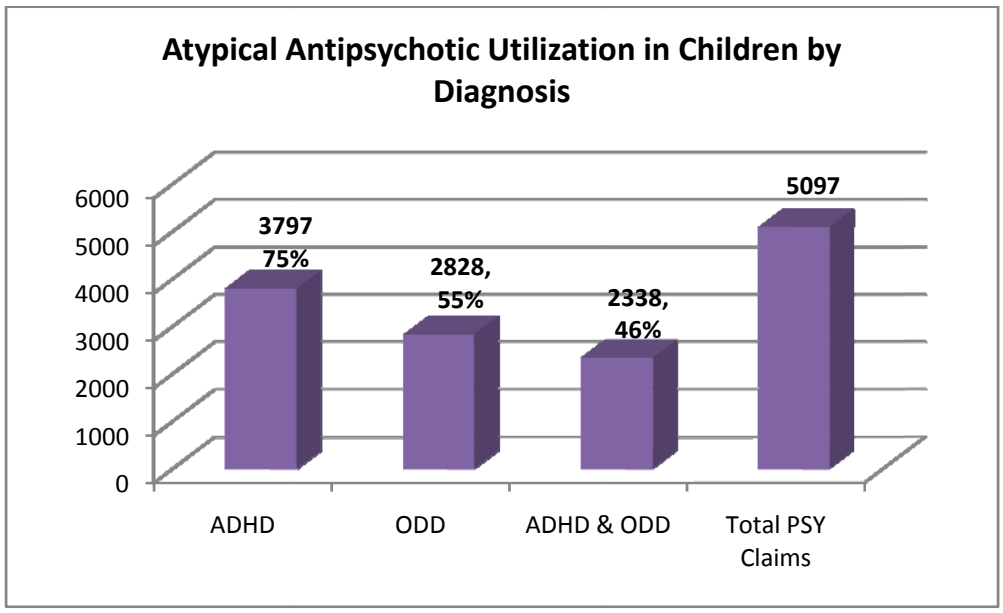
Based on currently available information, health care professionals should not change their prescribing practices for statins and patients should not change their use of statins.

Atypical Antipsychotic Utilization in Children for ADHD/ODD

At the September 25, 2008 DUR Board meeting, HID presented utilization data for atypical antipsychotics in children, presumably for attention deficit hyperactivity disorder (ADHD) and/or oppositional defiant disorder (ODD). Based on the information presented, the DUR Board presented some important questions regarding the use of these medications in children. This document serves to shed more light on this subject and the questions raised at the last DUR Board meeting.

Attention Deficit Hyperactivity Disorder vs. Oppositional Defiant Disorder

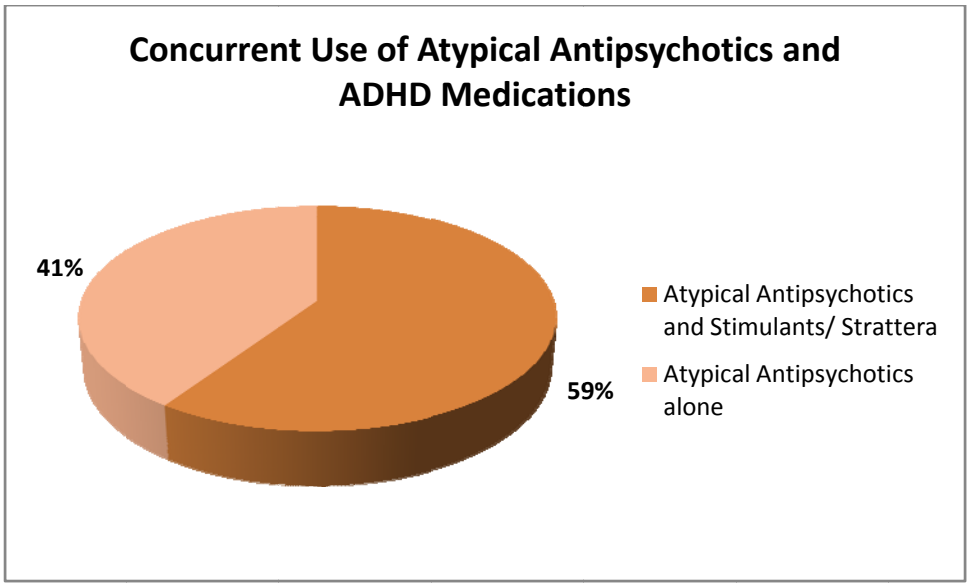
One question brought up at the September meeting was: What is the breakdown of pediatric beneficiaries receiving atypical antipsychotics regarding their diagnosis? Specifically, how many of these beneficiaries have an ADHD diagnosis, and how many have an ODD diagnosis?



As the chart above shows, 75% of all patients 18 years old or younger who received an atypical antipsychotic had a diagnosis of ADHD, while 55% had a diagnosis of ODD. 46% had both diagnoses, ADHD and ODD.

Concurrent Use of Atypical Antipsychotics and ADHD Medications

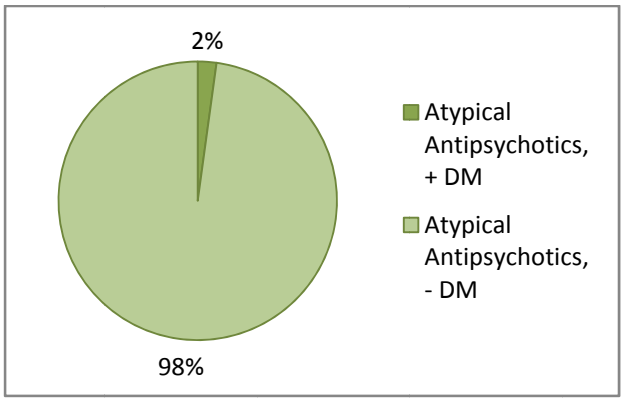
Another request made at the September DUR Board meeting was for the utilization data for pediatric beneficiaries with an ADHD and/or ODD diagnosis who had received an atypical antipsychotic concurrently with stimulants or Strattera®.



Of the 4287 beneficiaries under the age of 19 who received an atypical antipsychotic and had a diagnosis of ADHD and/or ODD, 2550 (59%) also received treatment with a stimulant or Strattera®. This indicates that, although the use of atypical antipsychotics in pediatric patients for ADHD/ODD is off-label, the majority of providers treating these patients have attempted trials of conventional treatment modalities for these diagnoses and for whatever reason have had to continue on to other options.

Incidence of Type 2 Diabetes Mellitus

A final observation made at the September meeting was the increased risk of metabolic adverse effects when being treated with atypical antipsychotics. An analysis was done on the pediatric beneficiaries who received atypical antipsychotics to determine how many also had a diagnosis of Type 2 Diabetes Mellitus, one of the more common and frightening risks associated with these medications.



Only 2% of the pediatric beneficiaries with a diagnosis of ADHD/ODD who received an atypical antipsychotic also had a diagnosis of Type 2 Diabetes Mellitus. This should be encouraging to those who were worried that the incidence of Type 2 Diabetes would be higher in this population due to their use of atypical antipsychotics. However, the potential risk for metabolic side effects with the use of atypical antipsychotics must not be disregarded based on these results.

Conclusion

Based on the information presented above, the following conclusions can be made.

1) The vast majority (75%) of patients 18 years of age and younger who received an atypical antipsychotic had a diagnosis of ADHD.
2) The majority of these patients being treated with an atypical antipsychotic for ADHD have attempted or are currently attempting treatment with stimulants and/or Strattera, the conventional treatment options for this disorder.
3) A very small percentage of pediatric patients being treated with atypical antipsychotics have developed Type 2 Diabetes Mellitus, a troubling side effect associated with atypical antipsychotic use. However, this finding should not provide a false sense of relief to Board members, as these patients could still develop Type 2 Diabetes and other metabolic disorders later on, especially if treatment with these agents is continued.

Preventive Treatment of Migraine Headaches

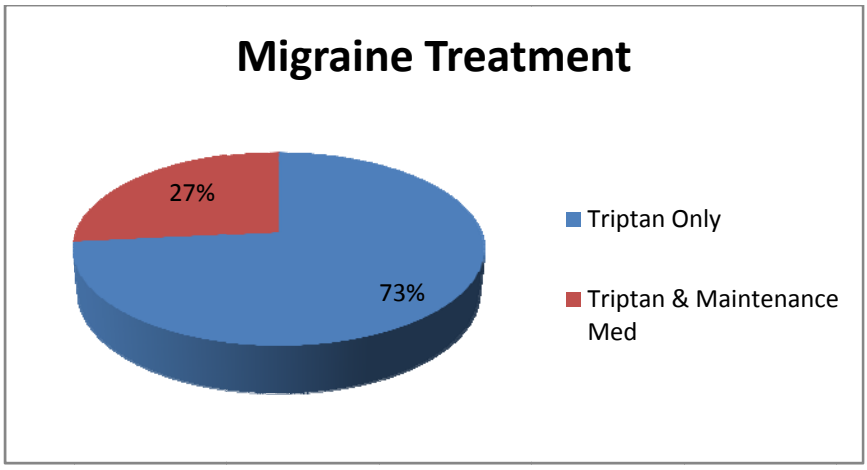
Migraine headaches affect approximately 28 million people in the United States. Migraines are a common type of headache, often accompanied by symptoms such as nausea, vomiting, or sensitivity to light. Many patients will complain of throbbing pain felt only on one side of the head. The pain associated with migraines can be disabling, making it difficult for patients to work or perform daily activities. These headaches tend to start between the ages of 10 and 46, and there may be a familial tendency associated with their occurrence. While the exact chain of events that lead to a migraines are not clear, some triggers include:

- Allergic reactions
- Stress
- Exposure to smoke
- Skipping or avoiding meals
- Alcohol

Migraines can last anywhere from 6 to 48 hours, with symptoms ranging from dull to severe. Most treatments associated with migraine headaches are considered rescue medications, including triptans and narcotic analgesics. However, there are some treatment options available that help prevent the occurrence of migraines. These include amitriptyline, propranolol, Topamax®, and Depakote®. HID conducted claims analyses to determine how many beneficiaries receiving rescue treatment with a triptan for migraines also received a deterrent medication.

Utilization data for the triptans and the preventive medications was gathered for a 6-month interval, from 3/27/08 to 9/26/08 (the most recent date for which claims data was available). These searches were then intersected to determine the number of beneficiaries who received both types of treatment versus those who received rescue medication only.

Triptan only	1236
Triptan and preventive medication	350



Based on the results provided, only 27% of beneficiaries who received treatment with a triptan as a rescue treatment also received medication to help prevent such attacks. Nearly $400,000 was spent on the triptans alone during this 6-month interval. On average, approximately 31 beneficiaries receive their rescue triptan prescription on a monthly basis for acute attacks. If the number of beneficiaries who received deterrent medication increased, they may benefit with fewer episodes of migraines, resulting in less pain and suffering. In addition, Mississippi Medicaid may realize some cost-savings by decreasing the need for the rescue medications, which can be costly. For example, the retail price (according to drugstore.com) of 30 tablets of propranolol 10mg is $12.99; the retail price of 9 tablets of Imitrex 50mg is $229.78. That is a potential cost savings of 95% per prescription of propranolol that prevents a beneficiary from needing their Imitrex for acute migraine attacks.

Recommendation

In an effort to increase the number of beneficiaries who may benefit from the use of a preventive medication for migraine headaches, HID recommends the review of a current RDUR criterion identifying those patients with a diagnosis of migraine and claims history of an acute migraine treatment, but no claims history of one of the preventive medications.

Duplicate Therapy with Sedative/Hypnotic Agents

Sedative/hypnotic agents are indicated for the treatment of insomnia, although the individual agents have differing mechanisms of action. While one agent, Rozerem®, interacts with melatonin receptors, the others (Lunesta®, zolpidem, and zaleplon) activate GABA receptors and exhibit effects similar to those seen with benzodiazepines. There is some concern, based on reports of utilization in individual beneficiaries, that these agents are potentially being abused. It has been discovered that some beneficiaries are receiving multiple prescriptions for different agents within this class.

HID analyzed claims data for 2 consecutive months to determine if there is misuse of the sedative/hypnotics occurring in the Mississippi Medicaid population, and if so, what the magnitude of the misuse is. Claims data for all of the sedative/hypnotic agents for July and August 2008 were gathered, and then intersected to determine if duplicate therapy with any of the agents was occurring.

Total Sedative/Hypnotic Agent Utilization					
	Zolpidem	**Lunesta**	**Rozerem**	**Zaleplon**	**Temazepam**
July	1310	262	109	4	838
August	1367	279	86	5	818

		Zolpidem	**Lunesta**	**Rozerem**	**Zaleplon**	**Temazepam**
July 2008	**Zolpidem**		8	6	0	5
	Lunesta	8		1	0	0
	Rozerem	6	1		0	2
	Zaleplon	0	0	0		1
	Temazepam	5	0	2	1	
August 2008	**Zolpidem**		7	3	0	10
	Lunesta	7		1	0	2
	Rozerem	3	1		0	0
	Zaleplon	0	0	0		0
	Temazepam	10	2	0	0	

Based on the total claims count for the sedative/hypnotic agents in July and August 2008, there does not appear to be widespread duplicate therapy with these agents occurring. For example, of the 1310 beneficiaries who received a prescription for zolpidem in July, only 10 (<1%) received another prescription of temazepam during the same time frame. However, based on the potential for addiction that is associated with this therapeutic class, coupled with the high costs of some of the sedative/hypnotic agents, a duplicate therapy edit at the point of sale may be warranted in this class. This would prevent beneficiaries from receiving multiple prescriptions of differing agents within the sedative/hypnotic class by requiring the physician to submit a prior authorization request explaining the need for the additional medication. HID recommends the implementation of such an edit in order to discourage the improper use of the medications in the sedative/hypnotic class.

Appropriate Use of Benzodiazepines

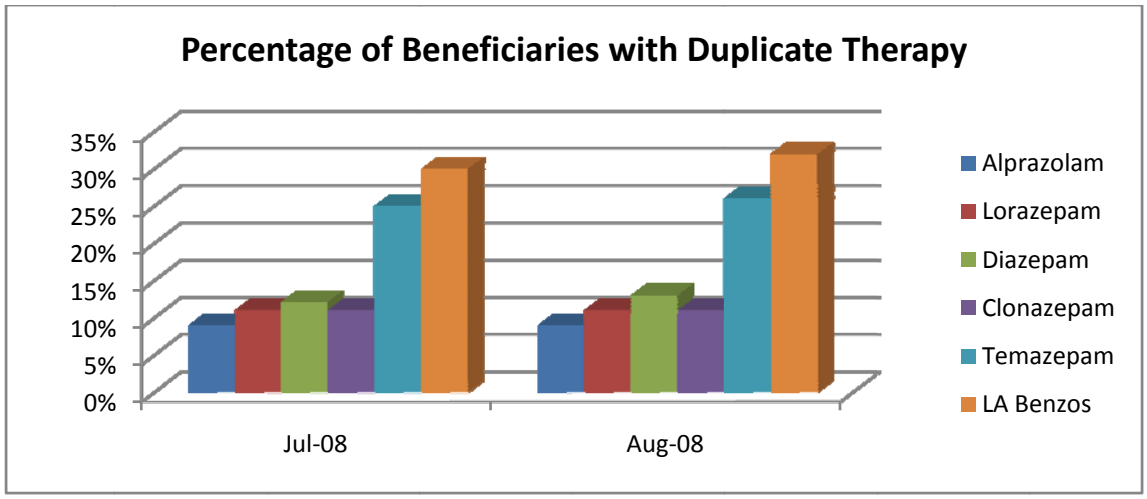
Benzodiazepines are agents used in the treatment of symptoms associated with anxiety disorders. According to the most recent treatment guidelines, these medications should only be used short-term in the management of anxiety disorders, and maintenance of these disorders should be managed with either a selective serotonin reuptake inhibitor (SSRI) or a serotonin and norepinephrine reuptake inhibitor. This information, coupled with the common knowledge that this therapeutic class is one that is often abused, led HID to conduct a claims analysis of the benzodiazepine agents.

Duplicate Therapy with Benzodiazepines

HID gathered utilization data for July and August 2008 for each of the benzodiazepines. This data was then intersected between all of the agents to determine how many Mississippi Medicaid beneficiaries received a prescription for more than one agent during these two months. The results are provided below.

		Alprazolam	Lorazepam	Diazepam	Clonazepam	Temazepam	LA Benzos
July 2008	Alprazolam		40	60	126	83	97
	Lorazepam	40		27	86	65	69
	Diazepam	60	27		54	30	33
	Clonazepam	126	86	54		48	55
	Temazepam	83	65	30	48		838
	LA Benzos	97	69	33	55	838	
August 2008	Alprazolam		39	67	131	86	101
	Lorazepam	39		20	90	69	73
	Diazepam	67	20		60	37	42
	Clonazepam	131	90	60		38	42
	Temazepam	86	69	37	38		818
	LA Benzos	101	73	42	42	818	

Based on these results, it is clear that there is some degree of duplication of therapy with benzodiazepines occurring in the Mississippi Medicaid population. For the short acting benzodiazepines (alprazolam, diazepam, lorazepam, and clonazepam), the rate varies from 10-15% depending on the agent. For the long-acting benzodiazepines (temazepam, triazolam, flurazepam, and estazolam), the rate of duplicate therapy with another benzodiazepine is much higher at approximately 30%. The chart below illustrates the degree of duplicate therapy for each agent.



Overutilization of Benzodiazepines

It was recently brought to the attention of the HID Clinical Staff that there are no quantity limits on the benzodiazepines. A provider in the mental health community voiced this concern due to numerous requests that they had received for large quantities of benzodiazepines on a monthly basis. With the utilization data gathered for the benzodiazepines for the previous topic, HID analyzed claims to determine the number of prescriptions of these agents that were for a large quantity. HID looked at the two NDCs of each agent with the highest utilization to determine the results of this inquiry. These results are provided below.

Qty	Alprazolam	Lorazepam	Diazepam	Clonazepam	Totals
>100	92	36	57	31	216
60-99	643	462	254	403	1762
30-59	168	374	86	217	845
<30	15	101	31	25	172

The results of this analysis show that there is a large prescription volume for excessive quantities of benzodiazepines, with nearly 66% of these prescriptions written for a quantity of 60 tablets or greater.

Conclusion

While benzodiazepines do have an appropriate role in the treatment of anxiety disorders, this role is limited and should be restricted to two to four weeks based on the most recent treatment guidelines for anxiety disorders. The results provided above show that there is some duplication of therapy with benzodiazepines occurring in the Mississippi Medicaid population, as well as potential overutilization of these agents. Both of these scenarios are troubling considering the abuse potential associated with this class.

Recommendations

Although the rate of duplicate therapy with the benzodiazepines is relatively small, it is still distressing when considering the abuse that is associated with this class. Edits at the point of sale that would halt the payment for duplicate prescriptions of benzodiazepines may need to be considered in order to curb the trend of duplicate therapy from growing.

Also, Mississippi Medicaid has made a strong stand in the past concerning agents that are commonly abused by beneficiaries by placing quantity limits on these agents in the hopes of discouraging their abuse. Therefore, HID suggests that the DUR Board consider recommending quantity limits on the benzodiazepines in an effort to avert abuse that may be occurring in the Mississippi Medicaid population.

Suboxone®/Subutex® Prior Authorization Process

Suboxone® and Subutex® are agents that are indicated for the treatment of opioid dependence. Both contain buprenorphine, an opioid agonist-antagonist that produces the same opioid agonist effects as other opioids but has a ceiling effect on these actions. Suboxone® also contains naloxone, an agent that is included to discourage the diversion and misuse of the buprenorphine component. When taken orally, naloxone has limited bioavailability; when crushed and injected, it will precipitate opioid withdrawal symptoms. Therefore, Suboxone® is the preferred agent when being used in an outpatient setting; Subutex® should only be administered in a supervised setting, due to the absence of naloxone.

Currently, Suboxone® and Subutex® require prior authorization for Mississippi Medicaid beneficiaries. HID, the prior authorization vendor, has noticed a significant increase in the prior authorization volume for these agents in the last few months. A review of utilization data for these agents confirms this observation.

Label Name	9/06-9/07 Rx Count	9/06-9/07 Total Remb Amt	9/07-9/08 Rx Count	9/07 - 9/08 Total Remb Amt
SUBOXONE® 8 MG-2 MG TABLET	475	$115,348.77	1778	$555,165.16
SUBUTEX® 8 MG TABLET	42	$17,894.25	98	$38,294.49
SUBOXONE® 2 MG-0.5 MG TABLET	6	$1,476.00	29	$8,281.42
SUBUTEX® 2 MG TABLET	1	$277.71	2	$528.02
TOTALS	524	$134,996.73	1907	$602,269.09

When compared to the same time period for 2006 – 2007, utilization has increased more than threefold, and the cost to the Division of Medicaid has increased by over 400% for these agents. While some of this growth can be attributed to increased marketing of the agents, such a large jump is troublesome.

The purpose of this presentation to the DUR Board is to gather insight from the members to determine if the current criteria being used for approval of Suboxone® and Subutex® are appropriate. Also, if there are additional recommendations that the Board members would like to suggest, HID and DOM are open to those as well.

Current criteria for approval of Suboxone® and Subutex® are:

For beneficiaries who have never received a prescription of Suboxone®/Subutex®:

- Provider must be listed on Suboxone®/Subutex® certified registry
- Beneficiary must have a diagnosis of opioid dependence

For beneficiaries who have received a PA approval for Suboxone®/Subutex® in the past:

- Review of paid pharmacy claims must not show any prescriptions for opioid analgesics
- Provider must be listed on Suboxone®/Subutex® certified registry

- Beneficiary must have a diagnosis of opioid dependence

Currently, these agents have DOM-implemented quantity limits of 62 tablets per 31 days. This is consistent with the recommended dosing according to the prescribing information, which states that the majority of patients can be maintained on 16mg/day (2 tablets/day). Any prescriptions over this amount require a Maximum Unit Override request from the prescriber.

Subutex® is only approved for pregnant patients. Since it is not recommended for use in an unsupervised setting, but is the recommended agent for pregnant patients, this is the only instance in which Subutex® is granted prior authorization approval.

Conclusion

As mentioned before, the Division of Medicaid would like to get input from the DUR Board regarding the prior authorization process for these agents. While these agents do provide a more cost-effective alternative for opioid dependency treatment, there is concern that they are not being used appropriately in some patients. It is the goal of the Division to ensure that the beneficiaries who truly need these products for treatment of their condition are able to receive them, and that they are used appropriately when prior authorization is granted.

MISSISSIPPI MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
4th QUARTER 2008

Recommendations	*Approved*	*Rejected*

1. Exenatide / Therapeutic Appropriateness _____ _____

Alert Message: Postmarketing cases of acute pancreatitis have been reported in patients treated with Byetta (exenatide). Patients receiving exenatide should be informed that persistent severe abdominal pain, with or without vomiting, is the hallmark symptom of acute pancreatitis. If pancreatitis is suspected all suspect drugs should be discontinued, diagnosis confirmed and appropriated treatment initiated. Exenatide should not be restarted unless an alternative etiology is identified.
Conflict Code: TA – Therapeutic Appropriateness
Drug/Disease:

Util A	Util B	Util C
Exenatide		

References:
Facts & Comparisons, 2008 Updates.
MedWatch: The FDA Safety Information and Adverse Reporting Program, 2008.

2. Becaplermin / Therapeutic Appropriateness _____ _____

Alert Message: An increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of Regranex (topical becaplermin gel) in a postmarketing retrospective cohort study. Use becaplermin only when the benefits can be expected to outweigh the risks. Use becaplermin with caution in patients with known malignancy.
Conflict Code: TA – Therapeutic Appropriateness **(Black Box Warning)**
Drug/Disease:

Util A	Util B	Util C
Becaplermin		

References:
Facts & Comparisons, 2008 Updates.
MedWatch: The FDA Safety Information and Adverse Reporting Program, 2008.
Regranex Prescribing information, 2008, Ortho-McNeil.

3. Simvastatin / Amiodarone _____ _____

Alert Message: Concurrent use of amiodarone and simvastatin may increase the risk of myopathy/rhabdomyolysis, particularly with simvastatin doses greater than 20 mg daily. Doses of simvastatin greater than 20 mg per day in patients taking amiodarone should be avoided unless the clinical benefit outweighs the increased risk of myopathy/rhabdomyolysis. Consider using an alternative statin (i.e., pravastatin, fluvastatin, or rosuvastatin) which is not metabolized by CYP3A4.
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Simvastatin 40 & 80 mg	Amiodarone	

References:
Facts & Comparisons, 2008 Updates.
MedWatch: The FDA Safety Information and Adverse Reporting Program, 2008.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2008.
Zocor Prescribing Information, June 2008, Merck & Co., Inc.

Recommendations ***Approved*** ***Rejected***

4. Simvastatin / Verapamil _____ _____

Alert Message: Concurrent use of verapamil and simvastatin may increase the risk of myopathy/rhabdomyolysis, particularly with simvastatin doses greater than 20 mg daily. Doses of simvastatin greater than 20 mg per day in patients taking verapamil should be avoided unless the clinical benefit outweighs the increased risk of myopathy/rhabdomyolysis. Consider using an alternative statin (i.e., pravastatin, fluvastatin, or rosuvastatin) which is not metabolized by CYP3A4.
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Simvastatin 40 & 80 mg	Verapamil	

References:
Facts & Comparisons, 2008 Updates.
MedWatch: The FDA Safety Information and Adverse Reporting Program, 2008.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2008.

5. Lovastatin / Amiodarone _____ _____

Alert Message: Concurrent use of amiodarone and lovastatin may increase the risk of myopathy/rhabdomyolysis, particularly with lovastatin doses greater than 40 mg daily. Doses of lovastatin greater than 40 mg per day in patients taking amiodarone should be avoided unless the clinical benefit outweighs the increased risk of myopathy/rhabdomyolysis. Consider using an alternative statin (i.e., pravastatin, fluvastatin, or rosuvastatin) which is not metabolized by CYP3A4.
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Lovastatin 60 mg	Amiodarone	

References:
Facts & Comparisons, 2008 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2008.
Mevacor Prescribing Information, Sept. 2008, Merck & Co., Inc.

6. Lovastatin / Verapamil _____ _____

Alert Message: Concurrent use of verapamil and lovastatin may increase the risk of myopathy/rhabdomyolysis, particularly with lovastatin doses greater than 40 mg daily. Doses of lovastatin greater than 40 mg per day in patients taking verapamil should be avoided unless the clinical benefit outweighs the increased risk of myopathy/rhabdomyolysis. Consider using an alternative statin (i.e., pravastatin, fluvastatin, or rosuvastatin) which is not metabolized by CYP3A4.
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Lovastatin 60 mg	Verapamil	

References:
Facts & Comparisons, 2008 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2008.
Mevacor Prescribing Information, Sept. 2008, Merck & Co., Inc.

Recommendations ***Approved*** ***Rejected***

5. Atorvastatin / Amiodarone _____ _____

Alert Message: Concurrent use of amiodarone and atorvastatin may increase the risk of myopathy/rhabdomyolysis due to inhibition, by amiodarone, of CYP3A4-mediated atorvastatin metabolism. Consider using an alternative statin (i.e., pravastatin, fluvastatin, or rosuvastatin) which is not metabolized by CYP3A4. If coadministration cannot be avoided, use the lowest possible dose of atorvastatin.
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Atorvastatin 20, 40 & 80 mg	Amiodarone	

References:
Facts & Comparisons, 2008 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2008.
Lipitor Prescribing information, Nov. 2007, Pfizer.

6. Atorvastatin / Verapamil _____ _____

Alert Message: Concurrent use of verapamil and atorvastatin may increase the risk of myopathy/rhabdomyolysis due to inhibition, by verapamil, of CYP3A4-mediated atorvastatin metabolism. Consider using an alternative statin (i.e., pravastatin, fluvastatin, or rosuvastatin) which is not metabolized by CYP3A4. If coadministration cannot be avoided, use the lowest possible dose of atorvastatin.
Conflict Code: DD – Drug/Drug Interaction
Drug/Disease:

Util A	Util B	Util C
Atorvastatin 20, 40 & 80 mg	Verapamil	

References:
Facts & Comparisons, 2008 Updates.
Micromedex Healthcare Series, DrugDex Drug Evaluations, 2008.
Lipitor Prescribing information, Nov. 2007, Pfizer.